VEPPANU™
vepdegestrant 200 mg 100 mg

DOSING AND ADMINISTRATION GUIDE

Information on dosing, administration, and management of potential adverse reactions with VEPPANU tablets

INDICATION

VEPPANU is indicated for the treatment of adults with estrogen receptor (ER)–positive, human epidermal growth factor receptor 2 (HER2)–negative, estrogen receptor 1 (*ESR1*)–mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

QTc Interval Prolongation

VEPPANU can cause QT (QTc) interval prolongation. Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to and during treatment with VEPPANU. Perform an ECG prior to initiation of treatment with VEPPANU and do not initiate VEPPANU in patients with QTc >470 msec. Repeat ECG approximately 4 weeks after initiating treatment and as clinically indicated. Avoid concomitant use of VEPPANU with strong CYP3A inhibitors or drugs known to prolong the QTc interval.

Please see Important Safety Information throughout and Full Prescribing Information at VEPPANUhcp.com

VEPPANU Offers a Convenient Treatment Regimen With Once-Daily Oral Dosing[1]

Same starting dose of VEPPANU for all patients—one 200-mg tablet daily

VEPPANU should be taken with food at approximately the same time each day

How patients should take VEPPANU

Patients should swallow VEPPANU tablets whole

- Tablets should not be chewed, crushed, dissolved, or split prior to swallowing
- Patients should not take VEPPANU tablets that are broken, cracked, or look damaged

What patients should do in the event the proper dose is not taken

Patients who miss a dose or vomit after taking a dose on a treatment day should take the next dose the following day at the regularly scheduled time.

Prior to initiation of VEPPANU:

- **Confirm presence of *ESR1*m**
- Correct electrolyte abnormalities
- Perform an ECG; do not initiate if QTc >470 ms and avoid concomitant drugs known to prolong QTc interval

~4 weeks after initiating VEPPANU (and as clinically indicated), repeat ECG.

No intramuscular injections or infusions

*ESR1*m=estrogen receptor 1 mutation; QTc=corrected QT interval.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, VEPPANU can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VEPPANU and for 2 weeks after the last dose.

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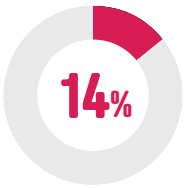
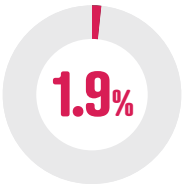
97% of Patients Stayed on VEPPANU Without Discontinuing due to ARs[1]

Low discontinuation and dose adjustment rates due to ARs

of patients discontinued VEPPANU



of patients needed dose interruptions



of patients needed dose reductions*

Adverse reactions that led to dosing modifications

- Permanent discontinuation occurred due to increased ALT and dyspnea (0.6% each)
- ARs that required dose reductions were electrocardiogram QT prolonged, fatigue, and musculoskeletal† pain (0.3% each)

Most common (≥10%) adverse reactions

The most common (≥10%) adverse reactions were decreased white blood cells, increased AST, musculoskeletal pain, fatigue, decreased hemoglobin, decreased neutrophils, increased ALT, increased alkaline phosphatase, nausea, decreased blood potassium, increased bilirubin, decreased appetite, electrocardiogram QT prolonged, decreased platelets, and constipation.

Other adverse reactions

- Serious adverse reactions occurred in 9% of patients who received VEPPANU, including any fracture (1.3%); fall, hypercalcemia, hepatic injury, pneumonia, musculoskeletal pain (0.6% each); and QTc prolonged (0.3%)
  - The largest mean increase in QTc interval was 12 ms (upper CI: 15 ms) at the recommended dosage of 200 mg once daily
- Clinically relevant adverse reactions in <10% of patients who received VEPPANU included headache, hot flush, diarrhea, vomiting, bradycardia, and urinary tract infection

Majority of adverse reactions were grade 1 or 2; none were grade 4

Study Design: The safety of VEPPANU was evaluated in patients with ER+/HER2– mBC following endocrine therapy in VERITAC-2. Patients received VEPPANU 200 mg orally once daily (n=312) or fulvestrant 500 mg intramuscularly on days 1 and 15 of cycle 1 and then on day 1 of each subsequent 28-day cycle (n=307).

*Dose reductions of fulvestrant were not permitted.

† Includes multiple related terms.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ARs=adverse reactions; BICR=blinded independent central review; CBR=clinical benefit rate; ORR=objective response rate; OS=overall survival; QT=QT interval; RECIST v1.1=Response Evaluation Criteria in Solid Tumors version 1.1.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Embryo-Fetal Toxicity (Continued)

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with VEPPANU and for 2 weeks after the last dose.

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Dose Modifications of VEPPANU Can Help Manage Adverse Reactions[1]

Recommended dosage modifications for adverse reactions

CTCAE Severity Grade	Dosage Modification
Grade 1	No dose modification is required.
Grade 2	Consider interruption of VEPPANU until recovery to grade ≤1 or baseline. Then resume VEPPANU at the same dose.
Grade 3	First occurrence: Interrupt VEPPANU until recovery to grade ≤1 or baseline. Then resume VEPPANU at the same dose or at the reduced dose at the discretion of the physician. If the grade 3 toxicity recurs, interrupt VEPPANU until recovery to grade ≤1 or baseline. Then resume VEPPANU at the reduced dose or discontinue VEPPANU at the discretion of the physician.
Grade 4	First occurrence: Interrupt VEPPANU until recovery to grade ≤1 or baseline. Then resume VEPPANU at the reduced dose. If a grade 4 or intolerable adverse reaction recurs, permanently discontinue VEPPANU.

VEPPANU Dose Reduction Levels		
Dose Level	**Dose and Schedule**	**Number and Strength of Tablets**
Dose reduction	100 mg once daily	One 100-mg tablet

If the reduced dose of 100 mg once daily is not tolerated, permanently discontinue VEPPANU.

CTCAE=National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS

Serious adverse reactions occurred in 9% of patients who received VEPPANU. The serious adverse reactions included any fracture (1.3%), fall, hypercalcemia, hepatic injury, pneumonia, musculoskeletal pain (0.6% each), and QTc prolonged (0.3%). Fatal adverse reactions occurred in 1.0% of patients who received VEPPANU, including dyspnea, cerebral ischemia, and unknown cause (one patient each).

Dose Modifications of VEPPANU Can Help Manage Adverse Reactions[1]

Recommendations for dose modifications in the event of QTc interval prolongation

QTc interval prolongation was reported in 10% of patients during the VERITAC-2 study.

- Grade 3 occurred in 1.6% of patients
- Dose reduction was required for 0.3% of patients due to QTc interval prolongation

QTc Prolongation*	Dosage Modification and Management
QTc >480 ms **or** >60 ms increase from baseline (and QTc ≤500 ms)	Withhold until QTc resolves to ≤480 ms **and** ≤60 ms above baseline, then resume VEPPANU at the same dose. Identify and treat reversible causes (eg, hypokalemia and hypomagnesemia). Initiate more frequent ECG monitoring.
QTc >500 ms	Withhold until QTc resolves to ≤480 ms **and** ≤60 ms above baseline, then: • resume VEPPANU at the same dose if reversible cause is identified and corrected (eg, hypokalemia and hypomagnesemia) • resume VEPPANU at the reduced dose if no reversible cause is identified Initiate more frequent ECG monitoring. Permanently discontinue if QTc >500 ms recurs.
Torsade de Pointes, polymorphic ventricular tachycardia, or signs/ symptoms of serious arrhythmia	Permanently discontinue VEPPANU.

No patients discontinued treatment due to QTc prolongation

*Heart-rate–corrected QTc using Fridericia's method.

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS (CONTINUED)

Permanent discontinuation of VEPPANU due to an adverse reaction occurred in 2.9% of patients, dosage interruptions of VEPPANU due to an adverse reaction occurred in 14% of patients, and dosage reductions of VEPPANU due to an adverse reaction occurred in 1.9% of patients.

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VEPPANU Dosing Adjustments for Drug–Drug Interactions[1]

Drug interactions that affect VEPPANU

Strong CYP3A Inhibitors	
Prevention or Management	• Avoid concomitant use of VEPPANU with strong CYP3A inhibitors in patients receiving VEPPANU 200 mg once daily. If concomitant use cannot be avoided, reduce VEPPANU dosage • Avoid concomitant use with strong CYP3A inhibitors in patients receiving VEPPANU 100 mg once daily
Mechanism and Clinical Effect(s)	• VEPPANU is a CYP3A substrate • Concomitant use with a strong CYP3A inhibitor may increase VEPPANU plasma concentration, which may increase the risk of VEPPANU-associated adverse reactions
Strong CYP3A Inducers	
Prevention or Management	• Avoid concomitant use with strong CYP3A inducers in patients receiving VEPPANU 200 mg once daily. If concomitant use cannot be avoided, increase VEPPANU dosage • Avoid concomitant use with strong CYP3A inducers in patients receiving VEPPANU 100 mg once daily
Mechanism and Clinical Effect(s)	• VEPPANU is a CYP3A substrate • Concomitant use with a strong CYP3A inducer may decrease VEPPANU plasma concentration, which may reduce the effectiveness of VEPPANU

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS (CONTINUED)

The most common (≥10%) adverse reactions, including laboratory abnormalities, were decreased white blood cells, increased AST, musculoskeletal pain, fatigue, decreased hemoglobin, decreased neutrophils, increased ALT, increased alkaline phosphatase, nausea, decreased blood potassium, increased bilirubin, decreased appetite, electrocardiogram QT prolonged, decreased platelets, and constipation.

VEPPANU Dosing Adjustments for Drug–Drug Interactions[1]

VEPPANU drug interactions that affect other drugs

Certain P-gp Substrates	
Prevention or Management	• Avoid concomitant use with certain P-gp substrates where minimal increases in concentration may lead to serious adverse reactions
Mechanism and Clinical Effect(s)	• VEPPANU is a P-gp inhibitor • VEPPANU increases exposure of P-gp substrates, which may increase the risk of adverse reactions related to these substrates
Certain UGT1A9 Substrates	
Prevention or Management	• Refer to the Prescribing Information for UGT1A9 substrates where minimal increases in the concentration may lead to serious adverse reactions
Mechanism and Clinical Effect(s)	• VEPPANU is a UGT1A9 inhibitor • VEPPANU increases exposure of UGT1A9 substrates, which may increase the risk of adverse reactions related to these substrates

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS (CONTINUED)

Clinically relevant adverse reactions in <10% of patients who received VEPPANU included headache, hot flush, diarrhea, vomiting, bradycardia, and urinary tract infection.

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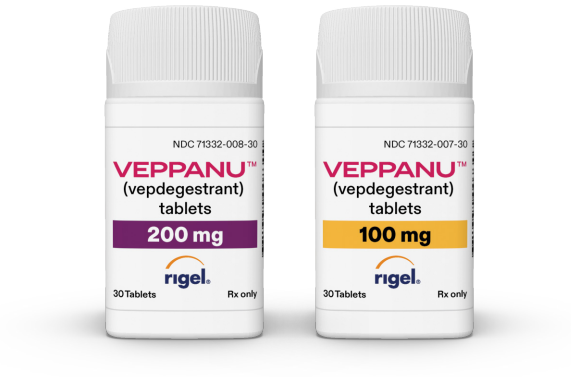
VEPPANU™ vepdegestrant 200 mg 100 mg

For 2L+ treatment of *ESR1*m, ER+/HER2– mBC regardless of menopausal status

A Once-Daily Tablet[1]



VEPPANU is available in 2 dose strengths

Recommended dose:
200-mg tablets
blue oval tablets, "VEP" debossed on one side and "200" on the other side

Dose for modifications:
100-mg tablets
blue round tablets, "VEP" debossed on one side and "100" on the other side

Convenient, room-temperature storage

- Store at 20°C to 25°C (68°F to 77°F)
- Excursions permitted between 15°C and 30°C (between 59°F and 86°F)

Learn more at VEPPANUhcp.com

RIGEL ONECARE provides support for patients taking VEPPANU

The Patient Support Team can assist you and your patients with understanding coverage, financial and copay assistance programs, and additional resources.

1-833-RIGELOC (1-833-744-3562) | Monday-Friday 8 AM - 8 PM ET
Visit RigelONECARE.com to learn more

Enroll Your Patients Today ▶

Reference: 1. VEPPANU™ [package insert] South San Francisco, CA: Rigel Pharmaceuticals, Inc.

IMPORTANT SAFETY INFORMATION (CONTINUED)

LACTATION

Advise lactating women not to breastfeed during treatment with VEPPANU and for 2 weeks after the last dose.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Important Safety Information throughout and Full Prescribing Information at VEPPANUhcp.com